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THE UNIVERSITY OF TORONTO MEDICAL JOURNAL

(An Undergraduate Publication)

This journal is published seven times a year, November to May, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to the student recent articles of scientific interest.

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Volume XIII — TORONTO, NOVEMBER, 1935 — Number 1

EDITORIAL

This issue marks the beginning of the thirteenth volume of the University of Toronto Medical Journal. The fact that the Journal has survived so long, and progressed to its present position, is sufficient evidence that it fills an essential place in student life. The primary function of the Journal is the publication of articles written by students. It is hoped that the existence of this medium for expression will stimulate some students to the performance of the literary and practical research necessary for the production of a really worth while scientific paper. Anyone who has undertaken to read the literature upon any medical subject realizes how important it is to know where and how to look for information. No student should graduate without having some knowledge of current medical literature. Writing for the Journal is one of the best ways of obtaining this knowledge.

A second, and scarcely less important, purpose of the Journal is to present authoritative articles upon subjects of recent interest to supplement the textbooks and lectures. These papers are especially valuable when dealing with

subjects upon which local teaching differs with that generally accepted, or with recent advances in knowledge not yet included in the text books. Many of the articles of this type are written by members of the staff. However, there is no reason why student articles cannot fulfil both functions if they are prepared with sufficient care. A student article can be comprehensive and reliable if the writer endeavours to consult all available authorities, and especially if he will consult members of the staff who are interested in the subject of the paper. Only by writing for it can a student take the fullest advantage of the opportunities afforded by the Journal.

WELCOME, '41!

Apparently Canada has at last turned the corner and prosperity has again become a reality, for how else could the class of '41 in Medicine be explained? In spite of the great increase in fees, the class is the largest to enter medicine at Toronto since the War. So the members of '41 are doubly welcome, both for themselves, and for the suggestion of returning affluence which they bring with them.

In so large a class the scholastic mortality next May much necessarily be high. Consequently those who wish to succeed will, more than ever before, need to 'hitch their wagons to a star.' Never aim to learn only what you are told in lectures, or forced to study in the laboratory. Always learn a little bit more than is expected of you. Begin at once to cultivate the habit of independent study. But remember that all knowledge is not to be found in the library. Supplement your scholastic endeavours with a study of human nature as seen in the many social and athletic activities of the University.

We, whose undergraduate days are almost over, envy you the pleasant years that lie ahead, and wish you the best of luck in both work and play.

NEW PROFESSORS.

This year four new professors have been added to the staff of the Faculty of Medicine. Dr. Alan Brown has been appointed to the new chair of Pædiatrics. This recognition of his services in the advancement of pædiatrics both in the University and throughout the city and province is certainly well merited.

Professor Andrew Hunter, for ten years professor of Biochemistry in this University, has returned to Canada, after an absence of six years in Scotland, to occupy the chair of Pathological Chemistry, left vacant by the death of Prof. V. J. Harding. It is a great pleasure to welcome Prof. Hunter back to the land of his adoption.

Dr. G. E. Richards has been appointed to the new chair of Radiology. His interest in the use of x-ray and radium in the treatment of cancer has been an important factor in the establishment of the Dunlap Building.

Dr. W. A. Scott has been appointed Professor of Obstetrics and Gynecology to succeed Prof. W. B. Hendry, who retired this year. It is with genuine regret that we record the retirement of Prof. Hendry, who has so ably filled this chair for the past thirteen years. However, we feel sure that the Department's excellent reputation will be maintained under Prof. Scott's very able guidance.

We wish to offer the congratulations of the students to each of these professors and to wish them every success in their new duties. We feel that the University is very fortunate in having such distinguished men upon its staff, for each one of these men enjoys an international reputation in his own field of science.

SOME RECENT ADVANCES AND EVENTS IN NEUROLOGY

By ERIC A. LINELL, M.D.,
Professor of Neuropathology, University of Toronto.

The writer was asked some weeks ago to write an article on Modern Trends in the Science of Neurology and, although he feels incompetent to perform such a task adequately, a brief review of some of the proceedings of various neurological meetings at which it has been the author's privilege to be present during the last twelve months, may prove of interest to the readers of the Journal. It is obvious that such a review must consist of personal impressions and must, therefore, be strongly biassed in the direction of the author's own interests. These must, perforce, be limited to only a few of the lines of investigation and research which the student of the nervous system may follow.

International Neurological Congress, 1935.

The Second International Neurological Congress was held in London during the first week of August, 1935, and was attended by about 800 men and women, very literally, from all over the world. There was consequently a very considerable confusion of tongues and, although the "official" languages in which papers could be given were limited to French, German and English, even this selection was too wide for some of us. London was selected as the place of meeting to form a suitable commemoration of the centenary of the birth of Hughlings Jackson. The mornings were devoted to formal discussions of major neurological problems. The subjects chosen were the epilepsies, the frontal lobes, the cerebrospinal fluid and the hypothalamus.

The epilepsies remain as one of the very dark spots in neurology, and it did not appear to the author that any new findings of interest were presented in the discussion of their pathological anatomy. Stress was laid on the multiplicity of the aetiological factors responsible for epileptic seizures and Dr. Penfield of Montreal gave his experiences of cases in which this factor was trauma of the cortical tissue. Encouraging results have been obtained by him, and by many other surgeons, following the excision of scar in the damaged brain-tissue. It was appropriate that this should have been the first discussion in a Congress held in honour of Jackson, whose name is perpetuated in the clinical entity of Jacksonian Epilepsy. The commemoration was further emphasized during the course of the Congress by Profesor Foerster of Breslau's Jacksonian Lecture, in which he dealt in detail, and in perfect English, with the results which he has obtained by electrical stimulation of the human cerebral cortex. He pointed out, in the course of his lecture, that the motor cortex is very definitely fatiguable by electrical stimulation, the stimulated area becoming completely refractory to further stimulation. He suggested that this phenomenon probably accounts for the transitory pareses and paralyses which are frequently observed to follow an epileptic seizure, during which violent stimulation of cortical nerve-cells is believed to occur.

The discussion on the functions of the frontal lobes consisted largely of reports on experimental stimulation and ablation of these portions of the cerebral hemisphere and gave an index of the immense amount of work which is being done in this field. These experiments naturally divide themselves into those dealing with the motor and

those concerned with the premotor cortical tissue. Considerable numbers of frontal lobectomies have now been performed in man, but, in view of the fact that these lobes are obviously previously damaged by the presence of tumour or other disease, it is difficult to assess the results of their removal from the viewpoint of disturbance of physiological function. A case of human bilateral frontal lobectomy was on the programme for report by Brickner of New York but, as far as the writer knows, the paper was not read. An interesting paper by Sachs of St. Louis gave his results of destruction of the function of limited areas of the cerebral cortex by removal of the overlying pia mater, from which the cortex obtains its sole blood-supply.

The cerebrospinal fluid was discussed to a considerable extent with reference to changes in its chemical constitution in different diseases. The anatomy and physiology of the fluid was reviewed by Weed of Baltimore. The discussion included hydrocephalus and its treatment and, later in the meeting, Putnam of Boston described a somewhat inconclusive series of cases in which infants, afflicted with this disease, had been treated by electrical coagulation of the choroid plexus of the lateral ventricle. Considerable stress was placed by Cairns (London), on interference with the venous drainage of the brain as a factor in the production of cerebral oedema.

The final major subject for discussion, the hypothalamus, was of particular interest to the writer. The widespread attention which this small area of the cerebral tissues has received within the last few years is sufficient index of its importance to the organism as a controlling centre of the vegetative functions. Kappers of Amsterdam reviewed the anatomy of the hypothalamic tissue, as it can be traced through the animal series, and his paper was followed by that of Le Gros Clark (Oxford), who described the present knowledge of its histology and connections in man. It is to be regretted that Cushing of Boston was unable to give his paper, as he has done a great deal to open up the very interesting question of the effects of pathological states of this area of the diencephalon. We were privileged during the Congress to see Hess' famous moving picture showing the results of electrical stimulation of the hypothalamus. He has devised an operation by which electrodes can be placed permanently in position in the cat's hypothalamus. The results of stimulation vary markedly depending upon the exact position of the points of the electrodes in the hypothelamic tissue.

In the afternoons short papers were delivered, the Congress being split up, for the purpose, into seven sections, whose meetings ran concurrently. These meetings were somewhat unsatisfactory, as the sections were separated from each other by considerable distances and there was no method of knowing at what times specific papers were being given in individual sections. Pathology, on the whole, appeared to the writer to be poorly represented in these papers. Opportunity was, however, offered to members to hear many of the leaders of neurological investigation discuss a bewildering variety of phases of the subject.

The evenings were mainly devoted to functions which were purely social in character but Foerster's Jacksonian Lecture was delivered at the Headquarters of the British Medical Association as an evening function and the Conversazione at the Royal College of Surgeons was accompanied by magnificent raspberries and cream and a series of scientific exhibits of particular interest to the writer. Among the latter were photomicrographs of the original preparations of nerve-endings in voluntary muscle, prepared by Kulchitsky about 1922. A wonderful series of photomicrographs of the nerve-endings and nerve-fibres in the human epidermis and dermis lead Wollard (Barts) to believe that the nerve-endings conveying sensations of cold have a specific histological structure, and that all the

branches of one nerve-fibre end in sensory-organs of the same histological type. There were also histological demonstrations of the innervation of cerebral blood-vessels by Williams (Manchester), and of the innervation of teeth by Stewart of the same University. A demonstration of the newer metallic staining-methods, as applied to cerebral tumour-tissue, came from Cooper of Manchester. There were dreadfully complicated instruments, apparently of a bio-physical nature, which were being skilfully kept under control by the Solandts (Toronto). The Buckston Brown Experimental Farm, which was originally Charles Darwin's home, contributed the results of some of the work which it is fostering in the field of experimental surgery and the Imperial Cancer Research Institute was responsible for a living culture of nerve-tissue and for a demonstration suggesting that the cells of malignant tumours do not receive a specific innervation.

Meeting of American and British Neurological Surgeons, 1935.

This meeting was held at the National Hospital, Queen Square, on the day following the closing of the Neurological Congress and was a very stimulating one, demonstrating the great importance of neurological surgery and the wide-spread field which it now covers.

Many of the major problems were reviewed by different speakers, one of the most dramatic of which was a paper by Dott of Edinburgh, who described a series of cases of aneurysm of the intracranical portion of the internal carotid artery, which had been successfully treated by ligature of this artery in the neck. In one instance the aneurysm ruptured, while the patient was in the out-patient department, and successful ligature of the artery was performed as an emergency procedure. These vascular abnormalities can now be visualized radiographically by the intra-arterial injection of physiologically-inert, radio-opaque substances. Arteriography, as it is called, was introduced a few years ago by Moniz of Lisbon. "Thorotrast," a radio-opaque solution of thorium dioxide, is now being introduced into the cerebral ventricles and this substance may replace the use of air in the technique of ventriculography. Papers dealing with the technique of treatment of brain tumour and of brain abscess were given respectively by McKenzie (Toronto), and Horrax (Boston). The application of extension to the neck in the treatment of fractures of the cervical spinal column was discussed by Coleman of Richmond, Virginia. A suitably weighted rope is attached to a pair of calipers, reminiscent of a pair of ice-tongs, the points of which are imbedded in the outer table of each parietal bone. The meeting was followed by an excellent dinner provided by the kindness of the British Neurological Surgeons.

Opening of Montreal Neurological Institute, 1934.

The author was privileged to be the representative of the University of Toronto at the official opening of this Institute in September last year. It was an occasion of great importance in the advancement of Neurology in Canada. The Director, Dr. Wilder Penfield, expressed the hope that the Institute would come to be considered as a Canadian Institution. The beautiful entrance-hall, of which the ceiling is a painting of a highly magnified view of a Golgi-stained section of the cerebellar cortex, has engraved in its stone-work the names of about a dozen of the "Masters" in Neurology. It was of interest to note that four of these investigators were still alive and active when the Institute opened. Cajal has died since that time, but Sherrington, Pawlow and Cushing were among the names and Sherrington and Pawlow took an active part in the proceedings of the International Congress this year.

A short session of scientific papers was held to commemorate the opening of the Institute, among the speakers being Fulton of Yale, Putnam of Bos-

ton, Bailey of Chicago, and McKenzie of Toronto. The chairman of this meeting was Gordon Holmes of London.

Meeting of American Association of Pathologists, 1935.

This meeting was held in New York and was of little interest from the point of view of neurology, with the extremely important exception that virus diseases were fully discussed.

Many of these comparatively newly-discovered diseases exert their effects mainly on nervous tissue. The outstanding important example is poliomyelitis and, at this meeting, further work was reported bearing on the spread of the virus from the mucous membrane of the nose, along the fibres of the olfactory nerves and thence through the nervous-tissue by the axones of the nerve-fibres. If, for instance, the olfactory tracts are cut, the virus is unable to travel beyond the portion of nerve-tissue which is still attached to the nasal mucous membrane. In other experimental animals a section through the thoracic spinal cord was shown to prevent the virus from reaching the lumbar region of the spinal cord. Apart from poliomyelitis a number of virus diseases were discussed which give, clinically, a picture of encephalitis. A very fine piece of research work is being carried on in the minute investigation of an outbreak of encephalitis, which occurred in St. Louis a few years ago.

The Inaugural Meeting of the Canadian Physiological Society, 1935.

And, finally, to bring this review home and up-to-date, the writer attended the birth of the Canadian Physiological Society in Toronto on the 19th of October, 1935.

Neurology was well represented. A description of some positive results of electrical stimulation of the caudate nucleus of cats was given by Professor Miller of Western University. Hall of Toronto described some apparently specific heart-lesions, produced in dogs by the prolonged administration of acetyl-choline. From McGill came a paper by Professor Babkin dealing with the effects of nerve-stimulation on the zymogen granules in the cells of the glands of the alimentary tract. The paper was illustrated by beautiful photomicrographs, prepared by Dr. Bowie of that University, of sections of glands in which the zymogen granules had been specifically stained.

The exact words of an old Signboard preserved in the Polperro Museum, Polperro, Cornwall.

ROGER GILES,

Surgin Parish Clark and Sculemaster, Groser and Hundertaker.

Respectably informs ladys and gentlemans that he drors teef without waiting a minit, applies lachers every hour, blisters on the lowest tarms, and vissicks for a penny a peace. He sells Godsfathers kordales, kuts korns, bunyons, docters hosses, clips donkies wance a munth, and undertakes to look after everybody's navls by the ear. Joesharps, penny wissels, brass kanelsticks, fryin pans, and other moosical hinstruments hat greatly reydooced figers. Young ladies and gentlemen larnes their grammur, and langeudge in the purtiest mannar, also grate care taken off their morrels and spelling. Also zarm singing, tavching base vile, and all other sorts of fancy work, squadrils, pokers, weazels, and all country dances tort at home and abroad, at perfeksun. Perfumery and snuf in all its branches. As times is cruel bad I beg to tell ee that i has just beginned to sell all sorts of stashonery, ware, cox, hens, vouls, pigs, and all other kinds of poultry, blackin-brishes, herrins, coles, scrubbin-brishes, traykel and godley bukes and bibles, mise-traps, brick-dist, whisker seeds, morrel pokkerankechers, and all zorts of swatemaits, including taters, sassages, ane other garden stuff, bakky, zizars, lamp oyle, tay kittles, and other intoxzikating likkers, a dale of fruit, hats, zongs, hair oyle, pattins, bukkits, grindin stones and other aitables, korne and bunyon zalve, and all hardware, I has laid in a large assortment of trype, dogs mate, lolipops, ginger beer, matches, and other pikkles, such as hepson salts, hoysters, Winser sope, anzetrar—Old rags bort and sold here and nowhere else, new laid eggs by me Roger Giles; zinging burdes keeped, such as howles, donkies, paykox, lobsters, crickets, also a stock of celebrated brayder.

P.S.—I tayches geography, ritmitmetic, cowsticks, jimnastics, and other chynees tricks.

MEDICAL SOCIETY NOTES

The regular weekly meetings of the Medical Society Executive have been the scene of considerable activity this Fall. Under the able direction of the President, Frank McInnis, plans for the year have gone forward rapidly. The At-Home Committee, under Wilf, MacIsaac, has arranged to have the Medical At-Home at the Royal York Hotel on the evening of February 7th, 1936. Mr. F. P. Dewar has been appointed Chairman of the Daffydil Committee. Daffydil, this year, is to be held on the 5th and 6th of March. Wally Scott, President of sixth year, has announced that the graduation banquet will be held on March 14th.

However, all the time of the Society has not been devoted to planning social activities. Arrangements for open meetings, to be held in the near future, have been made. The problem of bursaries for needy students has also received active consideration. The Society was able to set aside $1,100 for this purpose last year. This sum will be supplemented by a further amount from other sources and the whole will be awarded to students who are in financial distress, $100 being given to each student whose qualifications are deemed suitable.

MEDICAL SOCIETY EXECUTIVE---1935-1936

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THE MEDICAL ATHLETIC SOCIETY

The Medical Athletic Society is composed of: President, 6th year; Vice-President, 5th year; Secretary-Treasurer, 4th year; Representatives from 1st, 2nd and 3rd years.

It is the duty of these men, who are elected by the students, to carry on the activities of "Meds" in interfaculty competition.

A portion of the fee paid by each student to the Medical Society is turned over to the M. A. S. and in this way the latter is able to provide the teams with sweaters and whatever equipment is necessary. Besides this, the M. A. S. awards the medical letter to those who have played for three years on interfaculty or intercollegiate teams, or on a championship interfaculty team or to any 1st "T" holders.

With a faculty as large as ours and considering the reputation of "Meds" in university athletics, there is no reason why we should not be able to win our share of interfaculty championships. This is possible only if every student who is physically able turns out for one or more of the teams.

To first-year men, the importance of the latter should be emphasized, as the sooner they get into the spirit of the faculty the more they are going to enjoy the course. To those who feel that they have not time for athletics, it is necessary to point out that the development and keeping fit of the body is just as important as the development of the mind.

So far this year we are off to a good start with both the Junior and Senior rugby teams at the top of their respective groups, neither having lost a game to date. The soccer and volleyball and lacrosse teams are getting under way and soon there will be a call for players for basketball, baseball (indoor), water-polo, boxing, wrestling, fencing and hockey.

With the big registration in first year and the number of athletes in other years in the course, everything points to a most successful year. So let us all get behind "Meds" and let those who do not make the teams turn out and cheer the players on to victory with the good old

Epistaxis, Prophylaxis,
Coughs, Colds, Rales
Varsity Meds, Varsity Meds
Varsity Medicals
Torcular Herophili
Val sal val
Varsity Meds, Varsity Meds
Rah! Rah! Rah!

MUSIC IN THE UNIVERSITY

By H. V. RICE, '36.

Music has, in recent years, become one of the most important of the activities of Hart House. This increased interest in musical events, which has been so apparent in the University, is but a part of a movement which has affected the whole city. In fact, it seems probable that the work of Hart House has been am important factor in initiating this Musical Renaissance in Toronto. It is the purpose of these few lines to acquaint the students, especially those in the first year, with the many musical opportunities afforded by Hart House.

Music has become one of the most important of the activities of Hart House during recent years. With the

progress and increased interest shown in musical events in Toronto there has been a similar progress in the University. Possibly the activities of Hart House have had much to do with the former. It is the purpose of these few lines to acquaint the students, especially of the first years, of the form that the musical activities centred in Hart House takes. Some apology is necessary for taking space in a medical journal for this purpose, but since there are many who miss out on such things merely through ignorance of their existence, and who are otherwise interested, it is thought justifiable to bring them to attention.

On eight Sunday evenings during the winter months concerts are given in the Great Hall of Hart House. These concerts are very popular and tickets for them are not often left unused. They were started in 1922 on a purely experimental basis, and with a great deal of difficulty, for, at that time, it was not easy to get artists to give their services voluntarily. From a rather inauspicious start they have grown to be quite famous, and the difficulty now is, not to get performers, but to arrange the programmes so that no one is left out who wishes to assist. Close upon a thousand students and their friends listen to each of these concerts.

On those Sunday evenings when there is no concert given, songsters are held in the Music Room. These are to provide an opportunity for the men to hear, and sing, the finest of the folk songs, sea chanties and national music. The songsters are conducted by J. Campbell-McInnes, who is an authority on, and well-known interpreter of, this type of music. They are entirely informal; smoking is permitted; cocoa, pie and cake are served afterwards. No knowledge of music nor any training in singing is required; in fact, the less of these the more enjoyable are the songsters.

Each Friday at noon short songs are held in the East Common Room from 1.30 to 1.55. These are conducted by Ross Workman. Well-known tunes and popular pieces are the rule. There is no particular purpose to them except to give one a chance to vent one's feelings, and this is done with great gusto.

At 5.00 o'clock each Friday an hour's recital is given in the Music Room. These also are informal and smoking is allowed. There is a definite plan to these recitals. Those given before Christmas are illustrative of the development of music from early times to the present, with some attempt also to present music of a special character, as operatic or orchestral, or for stringed instruments. After Christmas the series is intended to present music of the different nations such as Italian, Russian, Scandinavian, and so on. At all of these well-known artists offer their services and the quality of the recitals is excellent.

This article would not be complete without some mention of the Glee Club of the University, which is known as the Hart House Glee Club. It is a relatively new organization, having been started only three years ago. In spite of its youth, however, it was one of the attractions at a Sunday evening concert last year, which is sufficient proof of its excellence. Any male member of the University is permitted to join, and if one has a desire to appear before an audience this is the opportunity. The Glee Club is at present conducted by Charles Peaker, who has certainly done very fine work in the short time he has been with it. The Sunday songsters and the Glee Club are particularly valuable because the student can take part in them himself. There is a certain amount of satisfaction in listening to some one else perform, but it does not approach the real enjoyment that doing the thing one's self provides. There is no more profitable way to spend an hour or two each week.

HEMIPLEGIA

EDWARD F. BROOKS, M.D., M.R.C.P. (London)

Hemiplegia may be defined as paralysis of one half of the body. The paralysis may not be complete and we then speak of it as hemiparesis.

To understand the possible locations of lesions which will produce damage to the motor nerves on their way to supply one half of the body, one must recall the pathway of the upper motor neurones. The cells of the upper motor neurones are located in the pre-central gyrus, the axones pass down as the corona radiata to the anterior part of the posterior limb of the internal capsule, then through the mid portion of the basis pedunculi of the mid brain, the basal portion of the pons and pyramid of the medulla, in order, to the lower part of the medulla, where the fibres cross to take up their position in the lateral column of the spinal cord on the opposite sisdse. The lesion of hemiplegia is usually somewhere from the cortex down to the point of decussation in the medulla, and the commonest site is in the internal capsule, where the fibres are so closely grouped. As the commonest lesion is a vascular one, it is essential to understsand the blood supply of the brain. As the greater part of the motor cortex, the corona radiata and the internal capsule is supplied by the middle cerebral artery and its branches, it is necessary to understand the anatomy of this artery in particular. The student should review these anatomical points in detail.

Realizing that the lesions causing hemiplegia may be in one of the above locations in the opposite side of the cerebrum or brain stem to the side paralyzed, one should try to localize the lesion and from the clinical syndrome present arrive at a conclusion as to the type of the lesion.

(a) Lesions of the Cortex.

1. Damage to the cortex by *injury* resulting in brain lacerations or extradural or intradural collections of blood may result in post-traumatic hemiplegia or hemiparesis.

2. The presence of a *tumour* overlying or in the region of the motor cortex will cause hemiplegia usually of slow onset, possibly accompanied by convulsion of Jacksonian type. Other signs of cerebral tumour such as headaches, choked discs, etc., may be present.

3. Abiotrophy of the motor cells due to some injury at birth, asphyxia neonatorum, prematurity, etc., results in what is called *infantile hemiplegia.* It is obvious that this type will show itself at an early age, the arm and leg on the affected side will be smaller and shorter and will show signs of a degree of spastic hemiplegia. This condition is a form of so-called Little's Disease.

4. Following an epileptic seizure a transient hemiplegia may be present, called *Todd's Paralysis* and in these cases a gross cortical lesion such as a tumour should be ruled out.

5. Hemiplegia due to a *vascular lesion* of the cortex shows certain features which may identify it. This is particularly so if the lesion is on the left side of the brain in a right-handed person, the hemiplegia will then involve the right face and arm and aphasia may be present; the leg usually escapes because the leg area in the cortex is near the vertex and is supplied by the anterior cerebral artery.

The aphasia need not be complete but may be limited to an inability to name objects. Hemiplegia with aphasia is due to a cortical lesion, usually thrombosis of the Sylvian branch of the middle cerebral artery. An internal capsule lesion may produce dysarthria but not aphasia. If the hemiplegia is on the left side it is more difficult to determine whether the lesion is in the cortex or internal capsule, but, if the leg escapes, a cortical lesion is suggested.

(b) Sub-Cortical and Internal Capsule Lesions.

This is the commonest site of a lesion for the production of hemiplegia. *Encephalitis, abcess, tumour, hemorrhage* into a *tumour,* and *vascular* lesions are the usual causes. Most hemiplegias are due to vascular lesions, in this region, of the deep perforating branches of the middle cerebral artery. As will be noted later, the lesion may be hemorrhage thrombosis, or embolus, or, in some cases, vascular spasm has been described as the cause. Recall that if the lesion extends back to the retro-lenticular portion of the internal capsule, there will be, in addition to motor signs, sensory changes and hemianopia.

(c) Lesions of the Mid Brain, Pons, and Medulla.

Hemiplegias due to lesions of the brain stem are usually accompanied by paralysis of a cranial nerve on the same side as the lesion (the opposite side to the hemiplegia) and the level of the lesion is determined by the cranial nerve which is affected. These are called crossed hemiplegias. *Vascular* lesions, *polio-encephalitis* and *secondary carcinoma* are the commonest causes. In a person of cancer age a crossed paralysis should be considered as possibly due to secondaries and a search for the primary lesion made.

Realizing that hemiplegia may result from the above causes and in the locations noted, the most common clinical pictures will now be discussed. namely,

Cerebral Apoplexy.

This term is applied to a sudden vascular lesion of the brain and the usual clinical picture is one of hemiplegia. As already noted, the lesion may be thrombosis, embolus, hemorrhage, or angiospasm. The nature of the onset, the degree of the coma, and the outcome of the case usually decide the cause.

In **embolus** there is usually a source of the embolus (bacterial endocarditis, fibrillation, etc.), and the onset is sudden; coma may be present but not profound; the paralysis may be temporary.

Thrombosis occurs at periods when the blood pressure is comparatively low, during sleep, exhaustion, cold, debility; the onset is slow, often with paraesthesia or numbness in the arm and leg; coma may not be present or may be short in duration. The paralysis may improve quickly with varying degrees of residual hemiplegia resulting. All slight apoplexies which survive the first ten days are due to thrombosis or embolus. It should be remembered that cases of hypertension are as likely to get thrombosis as they are to get hemorrhage, the condition of the artery being the deciding factor and reason for the lesion.

Hemiplegia due to **hemorrhage** often occurs during exertion; the onset is sudden, the coma profound, respirations stertorous, and perhaps Cheyne-Stokes in type; blood pressure rises higher and elevation of temperature is present. The general cerebral effect may be so marked that the hemiplegia may not be obvious. These cases are usually fatal in a few days. It should be repeated here that hemorrhage is usually preceded by a rise in blood pressure higher than that patient's usual pressure, whereas cerebral thrombosis is preceded by a lower blood pressure than the patient's habitual pressure.

It becomes important to try to differentiate the type of lesion as such procedures as venesection, lowering of systemic blood pressure will favour the occurrence of thrombosis. That the blood pressure is found above a physiological normal is no justification for assuming that it is above the patient's habitual level and drastic lowering by nitrites, etc., is courting trouble such as occurrence of, or increasing, thrombosis.

When the patient suffering from cerebral apoplexy is first seen, depending on the extent of the lesion, coma will be the presenting problem. The differential diagnosis of coma must be reviewed and the case becomes more difficult if the hemiplegia is masked by

a profound coma. A vascular lesion having occurred, the intracranial pressure rises, due to hemorrhage and oedema, or, in thrombosis or embolus cases, due to oedema alone. This rise in pressure produces ischaemia of the brain; the general circulation is stimulated and the blood pressure rises, and if this vasomotor mechanism should fail, death will soon result when the blood pressure is unable to keep up to the ever-increasing intracranial pressure. As it is this rapid rise in intracranial pressure which causes the coma, the coma will obviously be more marked and will be constantly present and more often result fatally in hemorrhage cases. The first point of importance then in diagnosis, is the consideration of the degree of coma. One will next note the blood pressure, pulse, respirations and temperature. Marked rise in blood pressure, rapidly rising pulse rate, stertorous breathing, perhaps Cheyne-Stokes in type, and a definite rise in temperature are all suggestive of hemorrhage. The patient will show asymmetry of the face and blowing out of the cheek on the affected side; there may be deviation of the eyes and it will be to the side of the lesion; the arm and leg of the paralyzed side will be limp and when passively raised will fall without restraint. If the patient is seen immediately after the onset, the arm and leg will likely be spastic with the deep reflexes increased, but soon the affected limbs will become flaccid and the reflexes become diminished or absent. The plantar reflexes will give the dorsiflexion response on the affected side or on both sides if the coma is marked.

If the patient survives this stage of the onset he passes into a second stage characterized by the regaining of consciousness. Some power may be noted but asymmetery of the face, particularly in the lower portion, will remain. For a week or so the limbs do not change, then the hemiplegic arm may start to creep up to a flexed position while the leg remains in extension. A certain amount of voluntary power returns, accompanied by some rigidity. Power to elevate the shoulder returns first, then abduction of the arm, then flexion of the arm and later flexion of the digits; extension remains powerless in a great number. The hand is able to grasp but that may be all. Early in the case this act may appear as the "grasp reflex" and is not a true voluntary act. If there is further recovery, elbow extension may be possible and extension either of wrist or fingers, but rarely both. Movement of extensors of the wrist may be seen but very often they are only acting as synergists and not as prime movers. In the leg, extensors recover first and a great number of patients are unable to dorsiflex the toes or foot. They may be able to stand but flexion may be absent. During all this time hypertonus is making its appearance. It compares in quality to the decerbrate rigidity of animals. Hypertonus makes its appearance selectivity in the muscles which recover first, and thus the arm for example, will tend to come up to a flexed position. Occasionally old hemiplegics may have the leg drawn up but it is only in senile, demented, bed-ridden patients, who have become so fixed, not by hypertonus, but by position and arthritis. The rigidity of hemiplegia is characteristic; if you bend the leg at the knee, there is rigidity for the first twenty degrees of flexion, and then the hypertonus disappears — the so-called clasp-knife rigidity. In this stage of hypertonus, the deep reflexes will be increased, knee and ankle clonus may be elicited and the plantar reflex will be dorsiflexion—the picture of an upper motor neurone lesion. The bladder and bowel function is usually only affected in the initial stage of coma.

Interesting phenomena which may appear at this stage should be mentioned here—the so-called associated movements. The paralyzed arm of hemiplegia may at times go into involuntary movements on such occasions as yawning or stretching. Also on any voluntary forceful movement of the good parts of the body, the paralyzed limb

may contract as long as the voluntary one. This occurs only in spastic hemiplegias and is useful in diagnosing from hysteria. These associated movements vary from time to time. Also in looking to the side of the paralysis the arm will extend to that side and vice versa. Forceful, voluntary movements will not change these movements and depend upon the direction of the head.

Prognosis.

In any case of hemiplegia the prognosis becomes important, as it is of prime interest to the relatives as to what is the immediate outlook and if the patient survives to the residual hemiplegic state, what is the chance for recovery. It will be judged from the above remarks that the prognosis depends upon one's ability to make an accurate diagnosis as to the type and extent of the lesion.

(1) The Age of the Patient.

Hemiplegias occurring in young people are most likely embolic, tumour, abscess or polio-encephalitis. In a person 30 to 45 years of age syphilis is a prominent cause and these cases of syphilitic thrombosis usually have a good outcome. In the middle or advanced stages the ultimate outcome is influenced by the fact that the primary cause is disease of the arteries and as this persists the patient is prone to further apoplexies or other cerebral effects such as dementia, etc.

(2) History of Previous "Strokes".

Patients who have survived previous thromboses are liable to a fatal cerebral hemorrhage. This may also occur shortly after a thrombosis, due to secondary hemorrhage in the area of softening produced by the thrombosis.

(3) Type of Lesion.

Cerebral apoplexy due to hemorrhage is usually fatal in the first few days. Thrombosis and embolus cases may survive. Deep coma persisting, stertorous respirations, marked increase in blood pressure, rapid pulse, high temperature and the type of onset make the immediate outlook bad. After the period of onset of the lesion, if the blood pressure is steadily rising, or should suddenly fall markedly, the case is likely in a terminal state. An onset of fibrillation is a sign of heart distress and influences and prognosis.

(4) Bloody spinal fluid makes the prognosis bad except in cases of spontaneous subarachnoid hemorrhage.

(5) Development of bed sores and urinary infections make the outlook unfavourable.

(6) Cases not showing signs of improvement in paralysis in two days will have some degree of residual defect.

(7) Cases going on to spastic stage with clonus, etc., will have residual paralysis and the degree of spasticity is an index of the probable degree of impairment.

Treatment.

Any person with arterial disease and hypertension should lead a regulated life. Exhaustion and dehydration should be avoided and the physician should be careful of drastic lowering of the blood pressure, which would leave the patient prone to cerebral thrombosis. In all cases of cerebral apoplexy the treatment is the same. You wish to keep up the general systemic circulation, so stimulation is in order rather than the use of depressing drugs. Strong sedatives such as Morphia are contraindicated. Do everything possible to keep up the heart's action and encourage circulation. Keep the head and shoulders up so as to encourage the return of the blood from the head. If there is stertor, turn the patient on his side. Enemas are preferable to strong purgatives. Venesection is a procedure resorted to far too often. This is done to lower the blood pressure, and as has been stsated, the rise in blood pressure is usually indicative of the body's attempt to keep the cerebral circulation adequate to still vital parts of the brain and the patient's life may depend upon this

mechanism, and therefore, do not remove it. Also Venesection in thrombosis cases may encourage further thrombosis. Venesection may be helpful in those cases with plethora and cyanosis and in such cases it helps by relieving congestsion and thus encourages circulation. Spinal puncture should be done as a diagnostic procedure and if blood is found, repetition may be beneficial in proportion to the degree of relieving the intracranial pressure. Cases surviving the first few days should have passive movements started to avoid static arthritis from rest adhesions. Massage and passive movements may be helpful in the recovery stage but electrical treatments are not indicated as they increase spasticity. The bladder should be carefully watched and the patient protected as nearly as possible from the formation of bed sores. The patient should be up as soon as possible and walking as soon as power permits. When active movements commence, they should be encouraged. Have the patient grasp a rubber ball for a period each day, changing the size of the ball as improvement takes place. Also have him move the hand across the table by a crawling action of the fingers with the good hand holding down the affected one. During this period of convalescence watch the position of the limbs and prevent deformities as far as possible. Occupational therapy is an important adjunct to one's therapeutic procedures in the restoration of a hemiplegic patient to social activity.

I have tried to outline the subject of hemiplegia as briefly as possible. Considerable detail has necessarily been omittedd, but I hope the above will assist the student in reviewing the subject in greater detail.

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THE STATE OF CALCIUM IN THE BLOOD

By G. W. MANNING, B.A.

The biological importance of calcium has been recognized since the earliest times. However, it is only comparatively recently that the element calcium has claimed much attention in the field of biological research, due to the realization of the close association between calcium metabolism and various pathological conditions. Its association with normal physiological functions such as bone formation, membrane permeability, coagulation of blood and milk, cardiac action, nerve impulses, nerve and muscle excitability, further suggest a more exhaustive search into the exact nature of this element.

The material gathered here does not represent an attempt to give a solution of any one particular problem concerned wth the metabolism of calcium, but rather a review of the work done by the various investigators with regard to the state in which calcium exists in the blood.

Absorption of Calcium.

Man derives calcium principally from milk, cheese, butter, eggs, green vegetables and nuts. This calcium in our food exists in both organic and inorganic combination. It is probable that the digestive changes convert it entirely into the inorganic form so that it is absorbed as calcium salts partly or completely ionized. A large part of the calcium in the intestine apparently remains in or assumes the form of insoluble salts, carbonate, phosphate and soaps and is excreted as such in the faeces.

In general calcium absorption is promoted by factors which tend to keep calcium in solution in the intestine and vice versa. If a large amount of phosphate is fed, the faecal calcium increases because more of the insoluble phosphate is formed just as an undue amount of calcium carries more phosphate through the intestines. On the other hand anything which tends to produce a more acid medium in the intestines exerts a favourable influence on calcium absorption because it transforms calcium phosphate, carbonate and soaps into soluble calcium salts and permits the elimination of more fatty acids in the free acid state.

With regard to the effect of Vitamin D on the calcium balance, opinion is divided as to whether this is brought about by increased absorption from the intestine or by some effect on the intermediary metabolism. Hart, Tourtellotte and Heyl state that it has no demonstrable effect on calcium metabolism, while Clark claims that it increases the diffusible fraction of serum calcium. It seems then that Vitamin D besides promoting absorption of calcium from the intestine, has an action in some respects similar to that of Parathyroid Hormone in increasing calcium solubility in serum.

The Blood Calcium.

The Calcium Content of Blood Corpuscles.—Very wide variations are found in the figures given for the calcium content of whole blood, serum, plasma and corpuscles. This is due to a considerable extent to untrustworthy methods of determination of blood calcium. It is now generally accepted that the calcium content of the blood corpuscles is negligibly small; values of approximately 0.3, Mgm. per 100 c.c. of cells are obtained by most recent workers. This figure probably signifies that the interior of corpuscles is practically free from calcium.

The Relation Between Plasma Calcium and Serum Calcium.—Most workers state that the calcium content of the

plasma is practically identical with that of the serum. However, there is considerable variation in the figures for plasma calcium, while for the serum calcium practically all reports in recent years set the limits of normal variation as 9 to 11 mgm. per 100 c.c. Consequently blood serum is the most satisfactory medium for calcium estimations.

In a given individual, under physiological conditions, the serum calcium concentration is extremely constant. During the terminal months of pregnancy the serum calcium shows a slight tendency to be subnormal. This appears to be in agreement with the calcium required for the skeleton of the foetus. In the cerebrospinal fluid only 5 to 6 mgm. calcium per 100 c.c. is found. Rona and Takahashi have shown that in normal blood serum there are two fractions of calcium, a non-diffusible fraction and a diffusible fraction which will pass through a membrane. Also they estimated this diffusible fraction to be of the order of 55 - 75% of the total serum calcium. This appears to be in agreement with the calcium content of the cerebro-spinal fluid. A great deal of the early work was spent in determining this "diffusible" calcium both in the cerebro-spinal fluid and in blood serum, subjecting it to dialysis and ultrafiltration methods. That there is a diffusible and non-diffusible fraction of calcium is fairly well accepted now but the great problem of the recent past and present is the exact nature or state of the calcium in both of these fractions. At present it is believed to be present in at least three forms:

(1) Un-ionized, non-diffusible organic compounds, approximately 45%.
(2) Un-ionized diffusible or dialysable inorganic compounds approximately 35%.
(3) Diffusible calcium, approximately 20%.

It is evident that there is more calcium in the blood than can be explained by the laws of simple solution. This has led some to conclude that part of the serum calcium is not in the form of ionized salts, while others believe that serum is a super-saturated solution of ionized calcium salts.

There is considerable evidence that from 3 to 5 mgm. of the serum calcium is loosely combined with the proteins and thereby held in solution. Csapo and Faubl have shown that when the serum proteins are precipitated, each fraction carries with it more or less calcium. Also Salvesen and Linder have shown that the calcium content of eodema fluid and serous exudates is higher than if these contained no protein. Many dialysis experiments in which serum has been dialysed against protein free solutions, have shown that 40% to 60% of the serum calcium is freely diffusible, a portion being apparently held back by the serum colloids. Loeb demonstrated this union with serum colloids to be a loose one. He showed that when dialysis of serum through collodion membranes was prolonged against large volumes of 0.8% NaCl or HCl solution of PH. 2.5 all of the calcium diffused out of the serum. As has already been mentioned, dialysis against distilled water removed only 55% to 75% of the serum calcium. Also Loeb showed, by experiments with isolated serum proteins, that "euglobulin," "pseudoglobulin" and perhaps albumin appear to alter the diffusibility of calcium through collodion membranes when dialysed against water at PH. 6-8. This is probably the result of the formation of "calcium proteinate." Although most workers hold that the non-diffusible calcium is bound to the various serum proteins Cameron and Moorhouse are of the opinion that the non-diffusible calcium is a specific compound whose formation is controlled by the parathyroid hormone.

Ham in reviewing the subject states — "assuming that the cerebro-spinal fluid represents that portion which is diffusible, it appears that the non-diffusible calcium of the serum is tied up in some manner with the parathyroid hormone, so that after the parathyroids

are removed most of the non-diffusible portion disappears. In this case the serum calcium would chiefly be composed of the diffusible fraction so that the serum calcium level would tend to approximate that of the cerebro-spinal fluid. Cameron believes that the parathyroids eleborate a hormone which controls the formation of a non-diffusible calcium compound in the blood and that this keeps the diffusible calcium compounds at a constant ratio with itself.

With regard to calcium proteinate it is estimated that 3.9 mgm. calcium is held in solution by protein in normal serum. The magnitude of this fraction must vary with the reaction of the serum. At the isoelectric point of the protein it vanishes; on the alkaline side of the isoelectric point it increases with the PH. In the opinion of Loeb and Nichols, the amount of non-diffusible calcium in any sample of serum depends on the total amount of calcium, the amount of serum protein and the PH. Although the nature of this non-diffusible fraction is by no means settled, the evidence to date seems to show that, at least in part, it exists in the form of a calcium-protein complex.

The Presence of Calcium Ions in the Blood Serum.

Many attempts have been made to measure the concentration of calcium ions in serum, or in its ultrafiltrates or dialysates. A great deal of confusion has arisen from the idea that diffusible calcium and ionized calcium are identical. All existing evidence seems to suggest that this is not so and that only a small proportion of the total calcium is in an ionized state. Klink has furnished evidence that the whole of the diffusible calcium is not ionized —by finding that some of the calcium in serum ultrafiltrates, as well as in serum, does not travel to the cathode in electro-dialysis. Assuming that the non-diffusible calcium is in a non-ionic state, it appears that the ionized calcium normally constitutes from 35% to 45% of the diffusible calcium taking the normal limits for diffusible calcium to be 4.5 and 5.5 mgm. per 100 c.c. The quantitative relationship between the various calcium states in blood can be represented by this equation:

Total serum calcium	=	diffusible calcium	+ non-diffusible calcium.
9—11 mgm.	=	4.5 mgm.	+ 4.7—5.75 mgm.
		(1) Ionized 2 mgm.	
		(2) Un-ionized.	

We have yet to account for the presence of some 2-5 mgm. per cent. of calcium in an un-ionized diffusible form. Greenwald has sugested that it is a compound similar to calcium citrate, quite slowly precipitated by oxalate or phosphate, in equilibrium with the ionized fraction, and in some way promoted or maintained by the parathyroid hormone. It is known that in the presence of citrate the deposition of calcium on rachitic cartilage in inorganic calcium containing solutions is inhibited. Shelling and Maslow have found that injections of citrate decrease the non-diffusible calcium of the serum, the citrate apparently taking calcium from the protein. This is of interest in considering the anti-coagulant reaction of citrate and agrees with the view of Loucks and Scott, that it is not the ionized calcium but some calcium complex which plays a vital part in the coagulation of the blood. Very delicate methods for the detection of citrate are now available, and by the use of such, Thunberg assures us that this puzzling diffusible calcium fraction probably is not a citrate, however similar it may be. He has shown that the citrate content of the human blood serum is too small to carry the amount of calcium involved.

In consideration of the work of Benjamin and Hess, it would appear that calcium is present in normal serum in at least four fractions, two of which

are diffusible and two non-diffusible. Of the diffusible calcium, about two-thirds is in the form of an absorbable calcium-phosphorus complex, the remainder consisting of calcium ions. Of the non-diffusible calcium about one-quarter is absorbable by barium sulphate, the remainder, which is not adsorbable, contains the calcium usually described as bound to protein.

Further work has been done with rachitic serum and it was found that the adsorbable calcium-phosphorus complex was greatly reduced. In later work, Benjamin has demonstrated that the epiphiseal cartilage of long bones, possesses the ability to adsorb the calcium-phosphorus from the artificial solutions as well as from serum. When this complex had been previously removed, by means of barium sulphate, almost no adsorption of calcium by the cartilage occurred. Conversely when adsorption was first carried out with cartilage, the additional calcium which could be removed by barium sulphate, was very small. Cartilage obtained from the epiphiseal junctions of rachitic long bones is capable of adsorbing the calcium-phosphorus complex from normal serum. Consequently this work suggests that normal calcification of bone involves the adsorption of the calcium-phosphorus complex of the serum by cartilage in the region of the epiphiseal junction.

The Influence of the Parathyroids.

Ham has stated that "at present the bulk of evidence favors the theory that the blood calcium consists of two portions, the non-diffusible and diffusible, and that the non-diffusible portion is controlled by the parathyroid hormone. Furthermore that the two are in equilibrium not only with each other, but also with the calcium of the bony reservoirs." Thus an increase in the amount of the parathyroid hormone would lead to a shift in the equilibrium so that the calcium ions would pass from the bone through the diffusible state to the organic compound controlled by the parathyroid hormone. This would have the effect of gradually depleting the bones if this condition was maintained. From studies of parathyroid tumour it appears as if this is what occurs. Numerous investigators have shown that the bones lose calcium after administration of the parathyroid hormone. Thus, because of the equilibrium, the parathyroid controlled fraction of the serum draws calcium from the bones but as soon as the calcium level is raised sufficiently, calcium is excreted in the urine. Consequently the calcium of the bones is gradually withdrawn and passed into the urine. This would be the effect of large, continuous injections of parathyroid hormone or the situation which develops in cases of parathyroid tumour.

Ham has postulated that the shift in calcium during the period of rise in the serum calcium level following a single dose of parathyroid hormone is this: that calcium from the bones, teeth, intestine and other body tissues augments the fraction of serum calcium in simple solution. This being passed on to the fraction controlled by the parathyroid hormone, will cause it to increase. The fraction controlled by the parathyroid hormone attracts calcium during the period of rise in the serum calcium level. This implies an arrest in calcification, a possible injury to other tissues because of a deprivation of calcium and a temporarily increased absorption from the intestine.

After hypercalcemia has been attained by the administration of a single dose of the hormone, the calcium level begins to fall. Probably due to the fact that the hormone is being eliminated, broken down or affected in some manner so that it no longer retains its former ability to attract or hold calcium. The calcium formerly held in solution by the effect of the hormone would then be liberated. This would cause a shift in the equilibrium in the direction opposite to that which occurred during the period of rise with the possibility of calcium being deposited in bones and other tissues, or excreted by the intestine or in the urine.

Ham and Portuondo have pointed out that as the serum retains only a small amount of the total serum calcium in simple solution it is evident that, if the release of calcium from the greatly increased fraction associated with the parathyroid hormone is at all rapid, calcium salts are deposited in the bones or excreted by way of the kidney or intestine, so that there is a distinct possibility of calcium salts being precipitated in the tissues. They demonstrated by experiments with rats, the deposition of calcium in the tissues when the calcium curve had attained its peak and was beginning to fall, a time that would correspond to the release of calcium from the parathyroid-controlled fractions.

Vitamin D.

Both administration of Vitamin D and sunlight promote the intestinal absorption of calcium and phosphorus and restore the concentrations of these elements in the serum to the normal level. In extremely high doses, irradiated ergosterol causes the calcium of the serum to rise far above the normal level, produces hypercalcification of the skeleton, and pathological calcification in other organs. From such evidence, Peters and Van Slyke have stated the possibility that Vitamin D, besides promoting absorption from the intestines, has an action similar to that of parathyroid in increasing calcium solubility in serum. Furthering this, Taylor and his co-workers have produced evidence that Vitamin D stimulates the secretion of the parathyroid glands. Johnston and King have also performed experiments which give support to this theory. These workers injected dogs with activated ergosterol and took samples of cerebro-spinal fluid and blood at intervals. In several experiments following the administration of activated ergosterol, a rapid rise in serum calcium followed, reaching a peak in 48 to 60 hours followed by a gradual fall. The spinal fluid calcium remained practically constant until the serum calcium reached the peak or nearly so, when increases in the spinal fluid calcium were observed. Correlating these results with the action of the parathyroid hormone on the serum calcium, they appear remarkably alike. Consequently Johnston and King have concluded that Vitamin D acts through the parathyroid hormone to influence a fraction of the serum calcium.

Summary.

I. Absorption of calcium apparently depends on
   (i) The nature of the food.
   (ii) The H-ion concentration.
   (iii) Vitamin D.

II. Calcium content of corpuscles is negligible.

III. The calcium content of plasma and serum is practically identical. However, considerable variations are found in plasma calcium. Hence the use of serum in calcium determinations.

IV. Calcium exists in non-diffusible and diffusible portions; the diffusible fraction being divided into an ionized fraction and an unionized inorganic fraction.

V. With regard to the non-diffusible fraction, it exists as "bound to protein" or as a specific compound whose formation is controlled by the parathyroid hormone.

VI. Calcium ions constitute approximately 35% - 45% of the diffusible calcium.

VII. It has been suggested that the remaining fraction of the diffusible calcium exists in an absorbable calcium-phosphorus complex.

VIII. The parathyroid hormone apparently controls a fraction of the serum calcium.

IX. Recent evidence seems to indicate that Vitamin D acts through the parathyroid mechanism.

PEPTIC ULCER*

By H. WINTER, '36.

A peptic ulcer may be defined as a localized loss of substance in the wall of the stomach or duodenum. Any portion of the stomach may be affected, but there is a predilection for the pyloric end. The vulnerable part of the duodenum includes the first part and extends into the second part as far as the entrance of the pancreatic and biliary ducts.

As one reviews the anatomy of the stomach and this part of small intestine, it is observed that they have features in common. Embryologically they are both developed from the fore-gut and receive blood supply from the same source, the coeliac axis.

More important is the fact that they are both subjected to the action of the acid gastric juice.

Clinically there are two types of ulcers.

1. The acute gastric or duodenal ulcer.
2. The chronic type. (Which is most important).

Incidence.

The prevalence of peptic ulcer as a disease entity varies in different parts of the world. It is interesting to note that, in Europe, its occurrence varies from nation to nation. Cecil indicates that peptic ulcer is more common in the northern than southern countries. Denmark is recorded as 16.7% as compared with Russia, where it is .2% The difference in incidence is probably due to dietetic factors and living habits, rather than to any constitutional abnormalities. America has an index of 1.3% as compared to that of 5% of population in England.

Another noteworthy point is that the anatomical position of the lesion varies also. In England gastric ulcers are relatively more common than duodenal ulcers. But on this side of the water, the opposite is the case. Miller analysed a series of 279 operatively proven peptic ulcers and showed the ratio of duodenal to gastric ulcers to be 4 to 1.

Young women between the ages of 20 and 30, especially those of neurotic and emotional types, are more subject to an acute type of gastric ulceration. On the other hand, Moynihan's statistics and others, show that the chronic type of duodenal ulcer is more common in males (ratio 2 to 1), in middle-aged group of 40 to 50 years.

Pathology.

Although the acute ulcer may be found in any part of the gastric mucosa, 90% of the chronic ulcers occur at the pyloric end of the stomach, in relation to the lesser curvature and the so-called "Magenstrasse" or gastric pathway. They occur more frequently on the posterior wall than on the anterior wall. Ulceration involving both posterior and anterior walls, or around the cardiac opening, does occur but is comparatively rare.

Distinction between gastric and duodenal ulcer depends upon their relation to the pylorus. The pyloric vein serves as a good guide at operation, since it forms a complete venous ring around the pylorus. The majority of ulcers in the first part of the duodenum are more on the anterior surface, 50% of them being within ¾" to 1" of the pylorus in the direct path of the acid gastric juices. The pyloric ring itself is involved in about 20% of cases.

Pathogenesis.

Many theories have been brought forth concerning the etiology of this abdominal condition, but to date there is no universally accepted theory. It is fairly well accepted, however, that primarily there must exist a focal area of

*Presented at a meeting of the Aesculapius Society.

devitalized mucosa—"A locus minoris resistentiae" which is secondarily acted upon by acid gastric juice which initiates a process of digestion and sloughing. The following are a few of the existing theories:

1. **Infective Theory.** — This theory propounded by E. C. Roseau is that of the "Elective Affinity" for gastric and duodenal mucosa of a strain of pathogenic, virulent, non-haemolytic streptocci. The bacteria primarily invade the mucosa and set free a toxin which causes localized necrosis of tissue; this in turn is digested, giving rise to an ulcer. He has been able to isolate organisms from surgical specimens and simultaneously find in the same patient, indentical organisms in infected foci, such as diseased tonsils, teeth, gall bladder and appendix. Haden has confirmed his work by inoculating rabbits with strains of streptococci from teeth of ulcer patients and producing ulcers in 53% of animals.

2. **Vascular Disturbances.** — Von Bergman suggests that a causative factor may be the production of a localized ischaemia due to spasm of the smaller arterioles. A more direct cause is that of chronic arteritis (endarteritis obliterans) which with super-added thrombosis produces a localized infarction.

3. **Neurogenic Theory.**—Ulcer is due to a lack of balance between the parasympathetic (vagus) and sympathetic nervous systems. Gray found that duodenal ulcer occurred in 10 out of 50 patients with functional disturbances associated with tobacco smoking and believes that the nicotine contained in tobacco affects the sympathetic ganglion cells.

4. **Cushing** believes that peptic ulcer may be associated with lesions in the diencephalon.

5. **Trauma,** and eating of irritating foods, especially those having a secretagogue action, by causing excessive secretion of gastric juice, has also been brought forward as a cause of ulcer formation.

That the actual eroding or digesting of the mucosa was due to the hydrochloric acid was shown by Mann and Williamson in their classical experiments—

1. The bile and pancreatic ducts were transplanted into the lower ileum with the production in 10 out of 31 animals of typical peptic ulcers; 5 of these were chronic. The duodenal secretions are alkaline and composed of biliary, pancreatic and duodenal secretions. It is their regurgitation back into the stomach which is believed by many to prevent ulcer formation in the normal.

Berg, deprived 16 dogs of their pancreatic juice by means of fistulae for periods ranging from 12 to 37 days and found ulcers in only 1 animal, which was jaundiced and had marked liver degeneration. In 8 animals no ulcers were found in the stomach or duodenum 61 to 273 days after complete pancreatectomy. He concluded from his results that there is a greater ulcerative tendency, after the exclusion of bile than after the loss of pancreatic juice.

Macroscopic Appearance.

1. **Acute Ulcers.**—The acute ulcers are frequently multiple, small, a millimeter in size. They are merely erosions of the mucous membrane, but may extend to the submucosa. The surrounding tissue shows evidence of a haemorrhagic infiltration.

2. **Chronic Ulcers.**—The size of the chronic ulcer varies from 1 to 2 cms. in diameter and is of a punched out character. The edge is sharp and the wall terraced, giving the inside of the ulcer a funnel or cone shaped appearance. The depth of the ulcer varies. It nearly always involves the muscular layer, but may extend farther to the serosal surface, which undergoes a fibrous thickening. In the smooth fibrous base vessels may sometimes be laid bare and there is evidence of haemorrhage.

Microscopic Appearance.

Boyd describes in chronic ulcer, 4 definite zones which are from within, outward—

1. A zone of inflammation composed of fibrino-cellular debris impregnated with polymorphonuclear leucocytes and covered over with mucus.

2. Zone of necrosis, composed of dead granulation tissue.

3. Zone of living granulation tissue.

4. Zone of scar or fibrous tissue.

The relation of chronic follicular gastritis to peptic ulcer is quite constant. Dr. Robinson believes that there is chronic follicular gastritis affecting the pyloric mucus secreting portion of the stomach in the vast majority of ulcer cases. Johnston, in a series of 37 surgical specimens, observed at T.G.H., found chronic follicular gastritis associated with duodenal ulcer on 18 occasions, with gastric ulcer on 3 occasions and with stoma ulcers on 4 occasions.

Balfour of the Mayo Clinic, believes that the only lesion of stomach and duodenum, which can be considered benign, in the sense that it is not, or does not become malignant is duodenal ulcer. On the contrary, any lesion on the gastric side of the pylorus may become malignant. The incidence, however, is low and the local authorities agree with Ewing in placing it at 5% of cases.

Clinical Features.

Peptic ulcer is characterized by chronicity, periodicity, pain in relation to meals, and sometimes haemorrhage.

Gastric Ulcer.

1. *Pain* usually comes on soon (½ to 1 hour) after eating and is relieved by alkali or milk.

2. *Characteristic food rhythm*—food—comfort—pain—comfort.

3. *Periodic Attacks* occur at weekly or monthly intervals.

4. *Pain and tenderness* are located in epigastrium just below or to the left of xiphoid. Pain extending to the back means penetration and is felt to the left of the spines of the 8th and 9th dorsal vertebrae.

5. *Appetite* is good.

6. *Vomiting*, which occurs at the height of pain, gives relief. The vomitus is bitter and contains large quantities of HCl.

7. *Haemorrhage.*—A. Haematemesis occurs in 33% to 50% of cases, may be "coffee ground" type when not profuse, or bright red when massive.

B. Occult blood in stools in latent cases.

Gastric analysis—Hyperacidity.

Duodenal Ulcer.

1. *Pain* is marked by a feeling of burning or fulness in epigastrium 2 or 4 hours after meals.

2. *Characteristic food rhythm*—food—comfort—pain, with "hunger pains," which are prevalent at night.

3. *Periodicity*—More periodic than gastric ulcer, having a seasonal relation—spring and autumn.

4. *Pain and tenderness,* right hypochrondrium at the parasternal line on level of transpyloric plane. Posterior projection to the right of the 9th and 10th dorsal spines.

5. *Appetite* is good.

6. *Vomiting*—usually absent, if present usually as a complication.

7. *Haemorrhage*—if present, nearly always intestinally, with occult blood in stools. Frank haemorrhage is rare.

Gastric analysis—Hyperacidity.

Diagnosis.

A history of long standing digestive disturbance, with periods of exacerbation between remissions. Tenderness over some spot in the epigastrium. Gastric hypersecretion found in the fasting stomach contents and after a test meal substantiate the diagnosis of ulcer. The X-ray is not only confirmatory, but diagnostic in the sense that one is able to anatomically differentiate gastric from duodenal ulcers. The gastric ulcer shows a delayed peristalsis and a filling defect (niche, cavity, etc.). Duodenal ulcer, hyperperistalsis and deformed duodenal cap. Although a barium series gives a typical picture, a reliable history with negative X-ray findings, would still justify treatment for peptic ulcer.

The outstanding feature in peptic

ulcer is "pain." This may vary from a mere sense of fulness to a true pain of a colicky nature. Theories advanced as to its causation are:

1. "**Hyperchlorhydria,**" excessive secretion of acid. Carlson, however, believes that this does not occur. By observing a patient with a gastric fistula, he showed that there was a continual flow of gastric juice 10 to 60 c.c. per hour in the absence of food or psychic stimuli. Hence there is always some acid acting on the ulcer and yet the pain is not continuous in the uncomplicated case. Hurst introduced 4 oz. of .5% HCl. into the stomach in several cases of gastric ulcer and produced no pain. On the other hand Palmer administered .5% HCl. to gastric ulcer patients, and was able to produce at will the typical ulcer pain in 95% cases. The pain was immediately relieved by alkali.

2. **Spasm of pylorus or hypertonus.**—Pyloric spasm due to the irritation of the ulcer has been advanced as another cause of the pain. It likewise is supposed to produce a gastric hyperacidity by the prevention of regurgitation of alkaline duodenal contents, back into the stomach. Berg believes that gastric acidity is regulated more by such factors as — the rate of secretion of HCl., the amount of mucus, degree of dilution and gastric mobility than by the regurgitation of alkaline duodenal fluids.

It is now known that all gastric and intestinal sensations arise in the sensory endings in the muscle fibres and are conducted by the nerves distributed to these fibres. A hollow viscus is sensitive to distension and spasm. Upon this muscle sense in the stomach are dependent the hunger sensations. Ryle believes it is highly probable that the painful sensations of peptic ulcer are muscular in origin, spasmodic or tonic in nature and bear no relation to the effects of the acid juice on the ulcer. The cause of the spasm is related to the inflammatory reaction occasioned with the ulceration which, extending to the muscle coat, causes reflex contractions in the neighbourhood of the pylorus. The effect of pyloric hypertonus is to produce an increase of intragastric pressure, and it is the stretching of the muscle fibres which is reflected in the sensation of pain. It seems highly probable that the relief from pain which follows the use of alkali is not due to the neutralization of the acid in the chemical sense, but to relaxation of the tonus and more rapid emptying of the stomach. Ryle suggests that alkali interacts with the acid to produce gas, which after it is belched up gives relief.

Differential Diagnosis.

Peptic ulcer is one of a large group of upper gastro-intestinal disturbances marked by a somewhat common symptomatology. They are usually designated by the patient as "stomach trouble." The group of conditions that must be differentiated from peptic ulcer are—

1. Gastric carcinoma.
2. Extra-gastric disease.
   (a) Chronic cholecystitis.
   (b) Chronic appendicitis.
3. Pelvic disease in female, e.g.,
   Chronic cervicitis.
   Chronic salpingitis.
   Cystic degeneration of ovary.
4. Gastric crisis.
5. Functional nervous indigestion.

Gastric Carcinoma—

1. Pain is constant, having no periodicity or food relations.
2. Loss of appetite, especially for meats.
3. Loss of weight and energy with a secondary anaemia.
4. Gastric analysis shows achlorhydria and presence of lactic acid or blood.
5. Hard mass palpable in epigastrium in many cases.
6. X-ray confirms presence of new growth.

Chronic Cholecystitis—Is a long-drawn out disease characterized by:

1. Easily satisfied appetite.
2. Intolerance for fried, fatty foods.
3. Flatulence after meals. There is

often a history of acute cholecystitis, biliary colic or jaundice.

Chronic Appendicitis — History of primary acute attack of appendicitis with recurrent pain and tenderness in the right lower quadrant or in epigastric region. Pain may be colicky and is frequently associated with nausea and flatulence.

Chronic Pelvic Disease in Female— Chronic pelvic disease may cause pain in right or left upper quadrant and an associated peptic history due to reflex gastric hypersecretion. It is, however, ruled out by pelvic examination.

Gastric Crisis—May show periodicity and chronicity, recurring at irregular intervals over a number of years with periods of good health between. They are characterized by belching, nausea with violent pain in epigastrium. Appears suddenly and disappears with or without treatment. Examination reveals Argyll-Robertson pupil, loss of reflexes and a positive Wassermann.

Functional or Nervous Indigestion— This condition is not uncommon but is one which should not be diagnosed until every possible cause has been carefully eliminated.

Complications.

1. Acute haemorrhage.
2. Perforation with general peritonitis.
3. Penetration with localized abscess formation with perigastric adhesions.
4. Stenosis.

Eliason and Ebeling in a desire to evaluate the relative occurrence and mortality of haemorrhage and perforation in peptic ulcer, went over all the records for 10 years back at Surgical Division C. Medical Clinic at the Hospital of the University of Pennsylvania and the Philadelphia General Hospital. The cases considered were those which showed gross evidence of haemorrhage as seen clinically by frank haematemesis or tarry stools. They found in a series of 546 duodenal ulcers, 107 or 19.5% of cases, and in 92 gastric ulcers, 36 or 39.1% of cases which went on to haemorrhage. It is noteworthy that the incidence of haemorrhage in gastric ulcer is twice that in duodenal ulcer.

Haemorrhage is diagnosed by the sudden vomiting of a large quantity of blood and the onset of shock. Steady increasing shock for no accountable reason indicates bleeding into the intestine and is followed by melaena.

Perforation—Of a total of 729 peptic ulcers, 546 were duodenal ulcer and of these 60 or 14% perforated. 183 were gastric ulcer and of these 14 or 7.6% perforated. The duodenal ulcer perforates more readily because of its position on the anterior surface and for the same reason, the majority of gastric ulcers that perforate are situated in the region of the pyloric sphincter on the anterior surface.

Following perforation the patient is not shocked. Moynihan prefers to use the term "prostration" to describe this state of the individual. In the analysis of 74 cases of perforated ulcer the lowest temperature recorded was 96 and highest 103; 38 cases had a pulse rate about 100 per minute; 46 had a systolic pressure above 100 mm. Hg. except 4, and 3 of these were seen not sooner than 18 hours after perforation and died. There is generally abdominal tenderness, rigidity, hyperaesthesia and hyperalgesia extending more to the right iliac fossa, due to the outpouring of gastric contents. Pneumo-peritoneum can occur in about 10 minutes after perforation, giving disappearance of liver dullness, verified by X-ray.

Penetration has occurred when a patient complains of pain going through to the back, which stays continuously. There is a leakage of gastric contents on to the pancreas, this becomes secondarily infected and a localized abscess forms which becomes walled off with adhesions, binding the stomach to the pancreas and neighbouring organs. The pull of fibrous strands tends to deform the stomach contour.

Stenosis is not an immediate complication and shows itself when symptoms tend to become constant or irregular, with increasing difficulty in gastric

evacuation. The signs of obstruction are vomiting of large quantities of undigested gastric contents every second or third day.

Treatment.

The treatment of gastric or duodenal ulcer is essentially the same. It is universally agreed that duodenal ulcer is a medical problem. Moynihan believes that *perforation* is preventable, providing treatment is adequate and does not permit progression of the ulcerative process.

The ordinary acute ulcer which is a mere erosion of gastric mucosa, heals rapidly, with ease. The chronic ulcer is more resistant to treatment.

Rest.—The patient should be put to bed for a period of weeks to months depending upon the individual case. Mental rest as well as physical rest is essential.

Diet should be—

1. Nutritious and of adequate caloric value.

2. Non irritating to the stomach—meats, gravies and condiments left out.

3. Easily digestible and calling forth minimum amounts of HCl.

4. Smoking should be prohibited.

The most important symptom to relieve is the pain, and this is done with suitably arranged diets and lots of alkali. The classical diets are those of Sippy and Lentharz.

A modified Sippy diet is the most satisfactory. The patient is usually starved for a day or two, after which if the ulcer is on the gastric side, a duodenal tube is passed (to give complete rest to the stomach). Treatment is initiated on the first day by giving 1 oz. of water followed by 4 oz. of milk, every 2 hours. This should be run in slowly, the fluid being slightly above body temperature to prevent the sensation of cold. The patient is fed every 2 hours from 6 a.m. to 10 p.m., with remissions in the afternoon. On the second day 6 oz. of milk is substituted; 3rd day 6 oz. milk and ½ oz. of cream, 24%; 4th day, 6 oz. milk and 1 oz. cream; 5th day, 6 oz. of milk and 2 oz. of cream; 6th day, 5 oz. milk and 3 oz. cream.

This is continued for 3 weeks. The caloric value of the above is about 2,500 cals. and may be increased by the addition of ½ oz. of lactose. Depending upon the severity of the case, some alkaline mixture may be given between feedings. A satisfactory powder is—

Sod. Bicarb. 2 parts.
Bismuth carb. 1 part.
Mg. O. 1 part.

With improvement, creamed soups, egg-nogs and custards are gradually substituted. After 3 or 4 weeks, the diet should be 3 small meals per day, containing cooked non-fibrous vegetables and stewed fruits, etc. A gastric analysis should be done every so often to determine the acidity. In 4 to 6 weeks the patient should be symptom free. If a cure is desired, the treatment must extend over months and thereafter the patient must be careful "of what he eats."

The Lentharz diet is not as popular as the Sippy diet. It extends over a period of 2 weeks and is built up slowly upon milk and eggs, which are given from the onset of symptoms. The feedings are chilled and eggs and milk are alternated every 2 hours, so that 2 eggs and 6 ozs. of milk are given in the first 24 hours. By the 6th day 7 eggs and 22 oz. of milk are given, following this the egg content is decreased and scraped beef substituted. After the second week the eggs are boiled and milk gradually increased to a quart. Soft articles of diet are gradually added to the regime.

Surgical interference as a therapeutic measure is life saving only when a catastrophy such as a perforation has occurred. It is also indicated when medical treatment has failed, after a fair trial, and more radical measures must be adopted.

The only complication which is a medical problem is acute haematemesis, the treatment of which is—

1. The patient (depending upon his blood pressure and pulse rate) should be put to bed in a modified Trendelenburg position.

2. Absolute rest.

3. Morphia should be given regularly except where the blood pressure is very low.

4. Repeated transfusions—300 cc.

5. Intravenous saline with 5% to 10% glucose.

6. If the patient is not too sick, a tube may be passed into the stomach, which is washed out with 20 cc. warm saline periodically. This treatment results in a mortality of 2.7%.

Acute perforation is indeed an abdominal emergency. Through the hole in the gut there is a rapid outpouring of gastric contents, which irritate the peritoneum, resulting in a generalized peritonitis. It is, therefore, extremely important that in a case of perforation diagnosis be made and the abdomen opened, as early as possible. Delay is fatal. In those cases where there is free fluid within the peritoneal cavity at operation, the morality is—

Under 12 hours, 14.9%.

12 to 24 hours, 55.5% (more than double).

24 to 28 hours, 57.7%.

At operation the ulcer is closed on its serosal surface. A gastroenterostomy (gastrojejunostomy) may be performed then and there or subsequently. This is the operation of choice in that it diverts the acid gestric juice away from the ulcerated area, allowing it to heal. Mann, of Mayos, showed that if he side-tracked the gastric juice of animals with peptic ulcer, the ulcers healed with remarkable rapidity. In 4 of his dogs the ulcer base was clean in 10 days, and there were signs of active epithtlial cell proliferation from the margins. The ulcers completely healed in 30 days.

The causes of post operative death in 650 cases calculated by Eliason and Ebeling are—

1. General peritonitis 59% cases.

2. Pulmonary complications 15.3% cases.

3. Subdiaphragmatic and hepatic abcess 4.9%.

4. Heart failure 4.6% cases.

5. Shock, 4.3% cases.

Operative results on delayed operations for perforation are not very encouraging and the ideal results, without a doubt, are to be obtained by prompt diagnosis and immediate operation.

The operation of choice in cases with pyloric stenosis depends largely on the degree of obstruction and the discretion of the surgeon, in that either a gastroenterostomy or partial gastric resection, may be undertaken. Where malignancy is suspected, the type of operation is partial gastrectomy. In this procedure the pyloric portion of the stomach is excised and duodenum sewn on to the remaining portion of the stomach. This operation has one advantage, in that it allows a free regurgitation of duodenal contents back into the stomach, neutralizing the acid gastric juices.

An objection to gastroenterostomy is the possible formation of a "stoma ulcer" at the artificial opening. This ulcer tends to give return of symptoms and may perforate or bleed, etc., as did the original ulcer, for which the operation was performed. The cure of this condition necessitates a second operation.

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BRONCHOGENIC CARCINOMA

By C. G. SMITH, B.A., M.Sc., M.D.

Bronchogenic carcinoma has grown very considerably in importance during the past thirty years. Rather than being considered a rare condition it is now looked upon as occurring with about the same frequency as carcinoma of the large intestine. The appreciation of its true importance is essential in order that early diagnosis may be facilitated and a greater opportunity be provided for successful treatment.

Incidence.

One case of bronchogenic carcinoma is met with in every hundred autopsies. Five to ten lung carcinomata occur for every ninety in the rest of the body. During the ten years, 1925 to 1934, of all cases coming to autopsy at the T.G.H. and showing one or other of bronchiectasis, lung abscess (not including multiple abscess), pulmonary tuberculosis, empyema and bronchogenic carcinoma, approximately 8.9% showed primary carcinoma of the lung. The condition is approximately three times as common in men as in women (R. M. Hill, '34). The age incidence is similar to carninoma in general, the majority of cases occurring between forty and sixty years, but one half of all cases occur before the age of forty-six. (Meakins, '34).

Etiology.

The fact that carcinoma of the lung has been increasing steadily in incidence at a rate much greater than carcinoma in general has led to considerable speculation and experimentation to determine the factor responsible. To briefly state the facts, it may be said that tuberculosis is not now regarded as a cause. Influenzal pneumonia or other diseases leading to lung fibrosis may possibly be a factor in the development of malignancy by disturbing lung structure so that cells regenerate in an abnormal environment. There is lacking positive evidence, however, to support this. Inhalation of irritating substances over a long period apparently does play a part in the development of carcinoma in the oft quoted case of the worker in the Schneeberg mine. The exciting factor here may be radio-active dust (Meakins, '33). With the present state of our knowledge it must be said, however, that, like carcinoma in general, the etiology of lung carcinoma is unknown.

Gross Pathology.

(1) *Hilus type* (90%).—

(a) Origin.—The origin of these cases is largely in the primary bronchi (about one half), the remainder arise in the main lobar divisions of the latter. The tumor will have its beginning outside the lung, in some of these cases, where it arises near the bifurcation of the trachea.

(b) Morbid Anatomy.—Through a bronchoscope the carcinoma is seen as a slight roughening of the mucous membrane or as a polypoid mass projecting into the lumen. Where advanced one may see complete stenosis of the bronchus. On section the tumor is seen as a solid greyish type of tissue infiltrating the bronchus wall forming more or less of a mass at the hilus and extending in finger-like projections peripherally in the wall of the bronchial tubes. The consistency of the carcinoma will vary with the cell type to be described.

(2) *Type occurring peripherally in the lung* (10%)—

(a) Origin.—The point of origin is the bronchial epithelium at any point as far distally as the respiratory bronchiole.

(b) Morbid Anatomy.—Here the carcinoma cannot be seen with the broncho-

scope, but with the X-ray it may be recognized as a nodule of varying size (0.5 to 20 cm.) tending to be circular but characterized by infiltrating strands extending from its surface. This is also the appearance on section. The varying consistency of the carcimona will again be dependent on the cell type. In certain cases that probably represent a more advanced stage, the growth extends to give a diffuse involvement of the lung, which is more or less lobar in distribution, and on section very closely resembles the grey stage of pneumonia.

Microscopic Pathology.

The cells which line the respiratory tree and form its glands are all derived from the epithelial bud that develops from the primitive foregut to form the trachea and lungs. It is not surprising therefore that when these cells assume a malignant character they show a considerable variation in structure even within the same tumour, depending on the local environment and rate of growth. In the majority of cases, however, one type predominates so that on this basis the tumors may be described as consisting of (1) undifferentiated cells, (2) squamous cells or (3) cylindrical cells. We will consider these three types in order.

(1) *Undifferentiated cell type.*—This is found mostly in tumors at the hilus, the cells may be very small, closely resembling lymphocytes, with scanty cytoplasm and deeply staining nuclei (oat-celled carcinoma), or they may be large and polyhedral or spindle shaped. These cells are arranged in solid masses with a framework of irregular bands of connective tissue, in which lie the blood-vessels of the tumor. The proportion of connective tissue varies; it may be scanty or be so abundant as to form a scirrhous type of carcinoma.

(2) *Squamous cell type.*—This is also found mostly in tumors at the hilus. It may consist of cornifying or non-cornifying cells, the latter merging with the undifferentiated cell type. The cells are large polygonal or spindle shaped with scanty, pale staining cytoplasm and a large hyperchromatic vesicular nucleus occupying the greater part of the cell. There is no orderly arrangement, the cells grow in irregular masses forming whorls with central cell nests and not infrequently characteristic epithelial pearls.

(3) *Cylindrical cell type.*—The type in which this cell prevails is found in most cases of tumor remote from the hilus. It is composed of tall columnar, cuboidal or rounded cells. The structure is highly variable. The tumor may consist of gland-like spaces lined by two or three layers of cells and filled with mucin and cell debris. In some areas papillary projections into these spaces may be found. Again the cells may be arranged in columns or strands, which show anastomosis and branching but are devoid of lumen. The stroma consists of loose oedematous tissue, infiltrated with small, round cells. The above adenocarcinomatous variety frequently shows a tendency to spread by growth along the walls of the alveoli,

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lining them with a layer of columnar epithelium.

Spread of Bronchogenic Carcinoma.

(1) *Regional extension.*—Where the tumor is at the hilus there is a marked tendency to spread by direct growth along the lymphatics of the bronchi and the blood-vessels to the mediastinum. The heart and pericardium are commonly involved. The growth may extend to involve the superior vena cava and the pulmonary veins and arteries. It may cause a compression of these structures or more commonly invade the walls and give rise to neoplastic thrombus. The oesophagus and trachea may be compressed and infiltrated giving rise to dysphagia, and stridor. Involvement of regional nerves by pressure and infiltration, leads to recurrent laryngeal paralysis, to pupillary inequality (due to involvement of sympathetic nerves), and to pain along the intercostals (Fried, '31). Quite rarely direct extension to the thoracic wall may occur.

(2) *Metastasis.*—Metastasis is the rule in carcinoma of the lung. Klotz, '27, found metastasis in 23 of 24 cases. The spread may be either by the lymph or blood stream.

The location of the metastasis is varied. It may give rise to secondaries in the lung itself. More frequently it spreads to the hilus and involves mediastinal and thence cervical, retroperitoneal, mesenteric and axillary glands. Where it erodes a blood vessel and spreads in this way it reaches distant points and may locate in many different sites. The commonest in order of frequency are the liver, adrenals, bone, kidney, and brain. (R.M. Hill, '34).

SECONDARY PATHOLOGICAL CHANGES IN THE LUNG PERIPHERAL TO THE CARCINOMA.

The changes in the lung as a result of the presence of the neoplasm are due either to the obstruction of a bronchus, partial or complete and to superadded infection. Thus we find collapse of lung, bronchiectasis, abscess formation and development of gangrene. Abscess may develop about a bronchiectatic cavity or as the result of an infection of a necrotic area of the tumour. The pleura is frequently involved, giving rise to pleurisy usually with effusion.

Relationship of Clinical and Pathological Findings.

(1) In the type of tumour associated with the hilus. Here the earliest change is a roughening and raising up of the mucous membrane of the bronchus, giving rise to irritation which leads to the development of a reflex nonproductive cough. If this area ulcerates, blood streaked sputum will occur or even a series of frank, minor haemoptyses. As the bronchial wall becomes more involved the lumen becomes narrower and finally complete occlusion with collapse of the lung occurs. Atelectasis is, however, symptomless, so that it can only be recognized by physical examination. In cases of partial obstruction stasis of air and interference with escape of secretions may lead to infection with development of bronchiectasis, septic pneumonia, lung abscess or gangrene, each with its own train of symptoms. In these cases the secondary condition may be diagnosed correctly but unless the case is carefully investigated the presence of the carcinoma may be missed.

(2) Type of tumour remote from the hilus. In its early stage this type is symptomless. At times, however, it gives rise to pain of a steady aching character deeply situated in the chest, tending to spread up to the shoulder blade of the same side and down the arm. (Paterson, '30). As this type of growth spreads it may involve a bronchus and then one gets cough, etc., as with lesions in the region of the hilus.

With any of these types of primary carcinoma a frequent complication is invasion of the pleura. This gives rise to a dry form of pleurisy which is recognized by the development of a characteristic sharp pleural pain. Later pleural effusion develops. The latter

may also arise aside from direct involvement of the pleura by the blockage of lymphatics at the hilus leading to a transudation of fluid into the pleural space. As the fluid increases in amount dyspnoea develops and becomes more and more marked. The fluid is sterile and blood-tinged and reappears in a few hours if removed. Dyspnoea in minor paroxysms may occur from spasm of the bronchus due to irritation where the tumour is located near the bifurcation of the trachea (Meakins, '33) or result, in minor degrees, from atelectasis or massive infiltration.

In addition to the above, spread of the tumour may lead to involvement of the recurrent laryngeal nerve and result in the development of hoarseness. Where it involves the superior vena cava either from without, by pressure, or from within, by neoplastic thrombosis, it will interfere with circulation and result in oedema of the upper part of the body.

Again in a considerable number of cases first symptoms may arise from a development of a metastasis remote from the lung. Rogers ('32) emphasizes this by his figures showing the relative incidence of the different kinds of symptoms at the onset. Thus 44% showed symptoms referable to the lung, 12% referable to the pleura, and 44% to metastasis (cerebral, bone, stomach, uterus).

Physical Signs.

The early cases with cough and sputum may show a slight diminution of movement, diminished vocal fremitus and diminution of breath sounds over the affected area as a result of partial occlusion of the bronchus. In the majority of cases, however, no signs of abnormality can be detected at this stage. As the case progresses signs of effusion may develop. Where signs of consolidation occur it may be due to malignant tissue, to atelectasis, or to secondary inflammatory and suppurative changes.

Diagnosis.

From the above it is evident that carcinoma of the lung must be suspected in all cases where symptoms pertaining to the lung and of uncertain origin develop in persons of cancer age. In addition, the lung must be investigated as a likely source of the primary in cases where symptoms point to a possible metastasis, e.g., in the brain. Of real interest, however, is the matter of early diagnosis, i.e., at the time when the tumour still remains localized and has not involved the peribronchial lymph nodes. To diagnose the

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tumour at this early stage it is necessary to have this condition in mind in those cases over thirty who develop a persistent cough lasting for weeks with or without a development of blood-streaked sputum (particularly where tubercle bacilli can not be found). The final diagnosis of early carcinoma can only be accomplished by instrumental and histological methods.

(1) *The X-ray.*—This is of little use for early diagnosis of hilus tumors because a shadow means an extension beyond the original site to involve the lung or peribronchial glands. Where the growth is of the obstructive type it may lead to early atelectasis and this may give the clue to the underlying condition.

(2) *Lipiodol.*—The use of this opaque substance will show a filling defect, which in the absence of any history suggesting the swallowing of a foreign body is almost diagnostic of carcinoma. It has the advantage of showing these defects in regions which would not be accessible to the bronchoscope.

(3) *The bronchoscopic examination.*—With the bronchoscope ninety per cent. of the carcinomata can be seen. They may be recognized as a macular or papillomatous change in the mucous membrane, with perhaps a tough woody quality of the tube. For verification a section may be removed for histological examination.

Prognosis.

The course of the disease thus far has been uniformly to a fatal termination. The average duration after the onset of pulmonary symptoms is about six months. Graham gives the average duration as under two years with occasional cases surviving up to five years.

Treatment.

Only two possibilities exist for the treatment of primary carcinoma of the lung, of which one is radiotherapy (either roentgen rays, or radium) and the other is excision. In regard to radiotherapy, T. A. Edwards describes the application of radon seeds to the tumor via the bronchoscope and through an opening in the chest wall, with some encouraging results. Deep X-ray therapy and radium treatment using large doses at a distance, as well as in the form of external plaques is apparently of little or no value. As for surgical excision two routes are available. 1. Removal through a bronchoscope. This method although it may serve for removal of early polypoid-like tumours, is not applicable, because of the difficulty of complete removal, to the larger number which are of an infiltrating character. 2. Wide dissection and removal through an opening made in the thorax. In all there are six cases in the literature in which the patient has survived at least one year after the removal of the carcinoma in this way. Evarts A. Graham, '34, reports a case in which he removed the entire left lung in April, 1933, the patient making a good recovery from the operation with a consequent freedom from lung symptoms and marked improvement in his general condition. This method of treatment apparently is today our one hope of complete cure. Unfortunately the operation has a high mortality and is only of value in cases diagnosed before spread to mediastinal structures.

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BOOK REVIEW

MAN AND MEDICINE—by Dr. Henry E. Sigerist of University of Leipsig. Translated by Margaret Galt Boise.

This book serves several fields—It reveals the relationship of medicine to cultural life and gives the medical student and layman an insight into the life of the medical man. Secondly, its discussion of the development of the fundamental facts of the sciences upon which the practice of medicine is built, gives medical students and physicians a most useful introduction to, or review of, his studies.

It is unfortunate that the price of this volume is rather high (about $4.50), for a single reading cannot possibly be exhaustive . Facts, interesting conceptions and unusual approaches to accepted theories abound.

The writer of this review was particularly impressed by the almost superhuman combination of abilities which the medical man should strive to possess.

As a soul-searching test for guidance before accepting medicine as a profession, Dr. Sigerist's book is beyond comparison with those of writers of fiction or the products of Hollywood directors.

J. P. Fletcher.

ODE TO SALICYLATES

A GRUDGE

O Salicylates, Salicylates
You are the sum of all my hates!
First you fill me up with gas;
Then you declare, "It shall not pass!"
You take away my appetite
And leave me empty in the night;
You make strange noises in my ears
And add new saltness to my tears.
My poor old olfactory nerves
You set to smelling in wild curves—
Each and everything you do
Adds to my loathing just for you!
But oh! When fevered joints do ache,
And toll from me begin to take,
No more my cankered lips cry hates—
Bring on, Bring on those Salicylates!